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TITLE: Method of treating estrogen receptor positive carcinoma

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CLAIMS:

What is claimed is:

1. A method of treating or inhibiting an estrogen receptor positive carcinoma in a mammal in need thereof, which comprises providing said mammal with synergistically effective amounts of a rapamycin and an antiestrogen in combination.

2. The method according to claim 1, wherein the rapamycin is rapamycin.

3. The method according to claim 1, wherein the rapamycin is a ester, ether, oxime, hydrazone, or hydroxylamine of rapamycini.

4. The method according to claim 3, wherein the rapamycin is a 42-ester or 42-ether of rapamycin.

5. The method according to claim 4, wherein the rapamycin is rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid.

6. The method according to claim 4, wherein the rapamycin is 42-O-(2-hydroxy)ethyl rapamycin.

7. The method according to claim 1, wherein the antiestrogen is tamoxifen, 4-hydroxytamoxifen, or clomiphene.

8. The method according to claim 1, wherein the antiestrogen is a non-uterotophic estrogen.

9. The method according to claim 8, wherein the non-uterotrophic antiestrogen is selected from the group consisting of raloxifene, droloxifene, idoxifine, nafoxidine, toremifene, TAT-59, levomeloxifene, LY-353381, CP-336156, MDL-103323, EM-800, and ICI-182,780.

10. The method according to claim 8, wherein the non-uterotrophic antiestrogen is a compound of formulas I or II having the structures ##STR66##

wherein: R.sub.1 is H, OH, carboalkoxy of 2-12 carbon atoms, alkoxy of 1-12 carbon atoms, halogen or mono- or poly-fluoroalkoxy of 1-12 carbon atoms; R.sub.2 is H, OH, carboalkoxy of 2-12 carbon atoms, alkoxy of 1-12 carbon atoms, halogen, mono- or poly-fluoroalkoxy of 1-12 carbon atoms, cyano, alkyl of 1-6 carbon atoms, or trifluoromethyl, with the proviso that, when R.sub.1 is H, R.sub.2 is not OH. R.sub.3 and R.sub.4 are each, independently, H, OH, carboalkoxy of 2-12 carbon atoms, alkoxy of 1-12 carbon atoms, halogen, mono- or poly-fluoroalkoxy of 1-12 carbon atoms, or cyano, with the proviso that, when R.sub.1 is H, R.sub.2 is not OH. X is H, alkyl of 1-6 carbon atoms, cyano, nitro, triflouromethyl, or halogen; n is 2 or 3; Y is a saturated, partially saturated or unsaturated 5-7 membered heterocycle containing a nitrogen, which may optionally contain a second heteroatom selected from the group consisting of --O--, --NH--, alkylamine of 1-6 carbon atoms, --N.dbd., and S(O).sub.m ; m is 0-2 or a pharmaceutically acceptable salt thereof.

11. The method according to claim 10, wherein the antiestrogen is (2-(4-hydroxy-phenyl)-3-methyl-1-[4-(2-piperdin-1-yl-ethoxy)-benzyl-1H-ind ol-5-ol or a pharmaceutically acceptable salt thereof.

12. The method according to claim 10, wherein the antiestrogen is (1-[4-(2-azepan-1-yl-ethoxy)-benzyl]-2-(4-hydroxy-phenyl)-3-methyl-1H-indo l-5-ol) or a pharmaceutically acceptable salt thereof.

13. The method according to claim 1, wherein the estrogen receptor positive carcinioma is of the breast or ovary.

14. The method according to claim 1, wherein the rapamycin is rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid, and the antiestrogen is (2-(4-hydroxy-phenyl)-3-methyl-1-[4-(2-piperdin-1-yl-ethoxy)-benzyl-1H-ind ol-5-ol) or a pharmaceutically acceptable salt thereof.

15. A method of treating or inhibiting estrogen receptor positive carcinoma of the breast in a mammal in need thereof, which comprises providing to said mammal synergistically effective amounts, of a combination of rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid and (2-(4-hydroxy-phenyl)-3-methyl-1-[4-(2-piperdin-1-yl-ethoxy)-benzyl-1H-ind ol-5-ol or a pharmaceutically acceptable salt thereof.

16. A method of treating or inhibiting estrogen receptor positive carcinoma of the ovary in a mammal in need thereof, which comprises providing to said mammal synergistically effective amounts of a combination of rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid and (2-(4-hydroxy-phenyl)-3-methyl-1-[4-(2-piperdin-1-yl-ethoxy)-benzyl-1H-ind ol-5-ol) or a pharmaceutically acceptable salt thereof.